Figure 1

WO 03/089585

MshC nucleic acid sequence of M. smegmatis

ATGCAATCGTGGTCGGCACCGGCGATTCCGGTGGTTCCGGGACGTGGCCCTGCGCTG AACCATGTACGTGTGCGGCATCACCCCATACGACGCGACCCATCTGGGTCACGCCGC GACCTATCTGACGTTCGACCTGGTGCATCGCCTATGGCTCGACGCCGGACACACCGT GCAGTACGTCCAGAACGTCACCGACGTGGACGACCCGTTGTTCGAGCGTGCTGAGC GCGACGCATCGACTGGCGACGCTGGGCGACCGCGAGACGCAGCTGTTCCGTGAG GATCGCCGAGGTCGTCGAGATGGTCGAGAAGCTGCTGGCCTCGGGTGCGCGTACA TCGTCGAGGACGCCGAGTACCCCGACGTGTACTTCCGCGCCGACGCCACCGCGCAG TTCGGGTACGAGTCCGGCTACGACCGCGACACCATGCTCACGTTGTTCGCCGAACGC GGCGGGGACCCGGCCCGGGCAAGTCCGATCAACTCGACGCGTTGCTGTGGCG CGCCGAGCGTCCTGGCGAGCCCAGCTGGCCTTCGCCGTTCGGCCGGGCCCGG GCTGGCACGTGGAATGTTCGGCGATCGCCCTGACGCGGATCGGCACCGGCCTCGAC ATCCAGGGCGGCGCACCTCATCTTCCCGCACCACGAGTATTCGGCCGCGCA CGCCGAATCCGTCACCGGTGAGCGACGATTCGCACGCCACTACGTGCACACCGGCA TGATCGGCTGGGACGGCCACAAGATGAGCAAGAGCCGCGGCAACCTGGTCCTGGTG TCGCAGTTGCGCCCCAGGGCGTCGACCCGTCGGCGATCCGGCCTCGTTCTCC GGGCACTACCGCGAGGACCGGTTCTGGAGCAACGAGGTTCTCGACGAGGCCAACGC GCGACTCGCGCGTGGCGCAGTGCCACCGCATTGCCCGAGGCGCCCGATGCGACCG ACGTGATCGCGCGCGCCGCAGTACCTGGCCGATGACCTGGACACGCCGAAAGCG CTTGCCGCACTCGATGGTTGGTGTACCGACGCGCTGTCCTACGGTGGGCACGACACC GAGTCGCCGCGCTCGTGGCCACCACCGTCGACGCGTTGCTGGGTGTGGACCTC

MshC amino acid sequence of M. smegmatis (PMshCMs)

MQSWSAPAIP VVPGRGPALR LFDSADRQVR PVTPGPTATM
YVCGITPYDA THLGHAATYL TFDLVHRLWL DAGHTVQYVQ
NVTDVDDPLF ERAERDGIDW RTLGDRETQL FREDMAALRV
LPPHDYVAAT DAIAEVVEMV EKLLASGAAY IVEDAEYPDV
YFRADATAQF GYESGYDRDT MLTLFAERGG DPDRPGKSDQ
LDALLWRAER PGEPSWPSPF GRGRPGWHVE CSAIALTRIG TGLDIQGGGS
DLIFPHHEYS AAHAESVTGE RRFARHYVHT GMIGWDGHKM
SKSRGNLVLV SQLRAQGVDP SAIRLGLFSG HYREDRFWSN
EVLDEANARL ARWRSATALP EAPDATDVIA RVRQYLADDL
DTPKALAALD GWCTDALSYG GHDTESPRLV ATTVDALLGV DL (SEQ ID
NO: 2)

Figure 2B

>cysS2: 1242 bp - M. tuberculosis -

atgcagtcgtggtattgcccaccggttccggtgttgccgggacgaggcccgcagctacgg ctgtacgacagcgccgaccggcaggtccgtccggtggcgcccggatctaaggccaccatg tacgtctgcgggatcacgcctacgacgccacgcatctgggccatgctgccacctatgtg acgttcgacctgatccatcggctgtggctggatctcggtcatgaattgcactatgtccagaacatcaccgacatcgacgatccactatttgagcgcgcggatcgcgacggtgtcgactgg cgtgaccttgcccaagccgaggtcgccctgttctgtgaggacatggcggcgctgcgggtg ctaccaccgcaagactacgtgggggccaccgaagcgattgctgaaatggtcgagctcatc gaaaaaatgctggcgtgcgggcggcctatgtcatagaccgggaaatgggagagtaccag gacatctacttccgcgctgacgccaccctgcagttcggctacgagtcagggtatgaccgt gacaccatgctgcggctgtgcgaggaacgtggcggcgatccgcggcgccccggcaagagc gacgaactcgacgcgttgttgtggcgggccgcgggcccggtgagcccagctggccgtcc ccgttcgggcctggccaggctaggcatgtcgagtgcgcagccatcgcgctcagtcgt at cgg a ag cgg cct cga cat cca ggg cgg tgg tag cga tct ga tctt tccg cac cac gagttcaccgctgcgcacgccgaatgtgtcagcggcgaacggcgattcgcgcggcactacgtg catgccgggatgatcggctgggacgggcacaagatgtcaaagagccgcgggcaacctcgtg ctggtgtcggcgctgcgtgcgcaggacgttgagccatcggcggttcggctgggtttgctcgccggacactaccgagccgatcggttctggagccagcaggtgcttgacgaggcgaccgcc cggctgcaccgttggcgcaccgcaaccgcacttcccgccggtccggccgcagttgacgtt gtcgctcgggtgcgccgctacctggccgacgatctcgatacgcccaaagcgattgccgcactggatggttgggtcaccgatgcggtggagtacggcggcacgatgccgggggcgccgaag ttggtggcgacggcgatcgatgccctgctcggggtggacctg

Figure 2C ·

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MshC amino acid sequence of M. tuberculosis (PMshCMtP1101)

MQSWYCPPVPVLPGRGPQLRLYDSADRQVRPVAPGSKATMYVCGITPYD ATHLGHAATYVTFDLIHRLWLDLGHELHYVQNITDIDDPLFERADRDGVD WRDLAQAEVALFCEDMAALRVLPPQDYVGATEAIAEMVELIEKMLACGA AYVIDREMGEYQDIYFRADATLQFGYESGYDRDTMLRLCEERGGDPRRPG KSDELDALLWRAARPGEPSWPSPFGPGRPGWHVECAAIALSRIGSGLDIQG GGSDLIFPHHEFTAAHAECVSGERRFARHYVHAGMIGWDGHKMSKSRGN LVLVSALRAQDVEPSAVRLGLLAGHYRADRFWSQQVLDEATARLHRWRT ATALPAGPAAVDVVARVRRYLADDLDTPKAIAALDGWVTDAVEYGGHD AGAPKLVATAIDALLGVDL (SEQ ID NO: 4)

Figure 2D

MshC amino acid sequence of Corynebacterium striatum (AAG03366) (PMshC-Cor.s-GB)

MHAWPDPSVPAVAGTPVPLKLFDTADQRVKEVDTTPDANGEVGMYVCGI
TPYDSTHLGHAATYLTFDLAQRQLLANGHKVHYVQNITDVDDPLFERAER
DGVDWRELGTSQINLFRSDMEILSVIPPCDYIGAMESVDEVIAMVQQLLDA
GAAYELDQGDIYASIDATEQFGYESNLDRATMEEYFAERGGDPDREGKRD
PLDALVWRGHREGEPAWDSPFGPGRPGWHVECSAIATNRLGSHFAIQGGG
SDLAFPHHEFSAAHAEAALKVERMAGHYVHAGMIALDGVKMSKSLGNL
VFVHKLSEAGHDPSAIRLAVFAGHYREDRDFSDAILAEAEERLTRWREQL
AGEVSEAEATEVVDKLRAILADDLNTPEALSLLDGAAGDCNQIIATALDGL
LGVRI (SEQ ID NO: 5)

Figure 2E

MshC amino acid sequence of Streptomyces coelicolor A3(2) (CAC36366) (PMshCScGB1101)

MHAWPASEVPALPGQGRDLRIHDTATGGPVTLDPGPVARIYVCGITPYD ATHMGHAATYNAFDLVQRVWLDTKRQVHYVQNVTDVDDPLLERAVR DGVDWTALAEQETALFREDMTALRMLPPQHYIGAVEAIPGIVPLVERLR DAGAAYELEGDVYFSVEADPHFGGVSHLDAATMRLLSAERGGDPDRP GKKNPLDPMLWMAAREGEPSWDGGTLGRGRPGWHIECVAIALDHLGM GFDVQGGGSDLAFPHHEMGASHAQALTGEFPMAKAYVHAGMVGLDG EKMSKSKGNLVFVSQLRREGVDPAAIRLTLLAHHYRSDWEWTDQVLQ DALARLDRWRAAVSRPDGPPAEALVEEIREALANDLDSPAALAAVDRW AALQQESGGTDIGAPGVVSRAVDALLGVAL (SEQ ID NO: 6)

Figure 2F

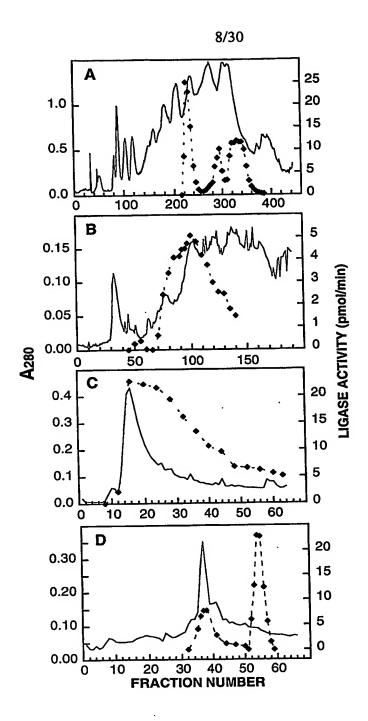


Figure 3

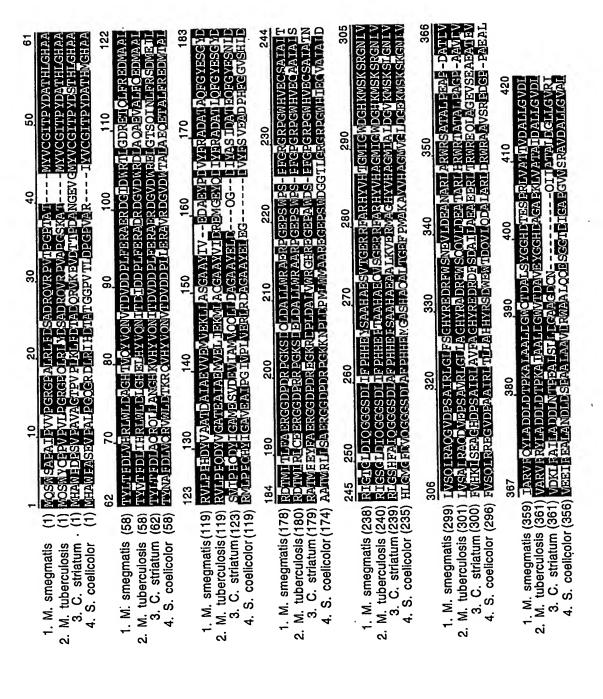


Figure 4

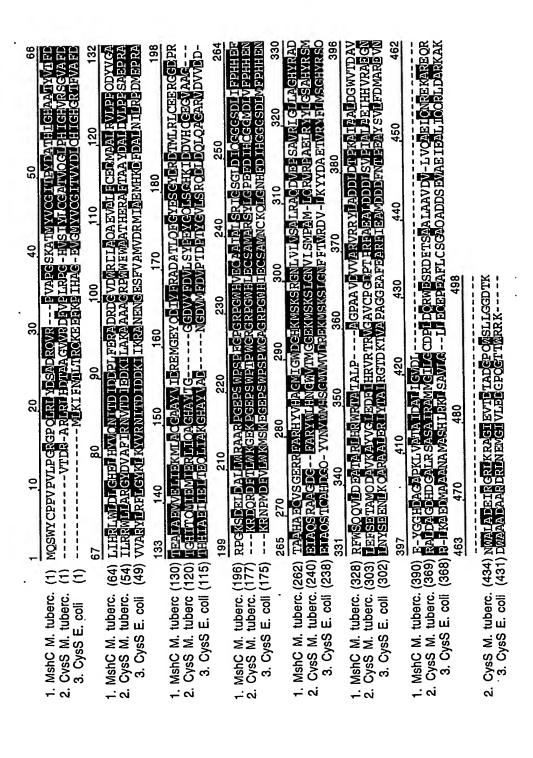


Figure 5

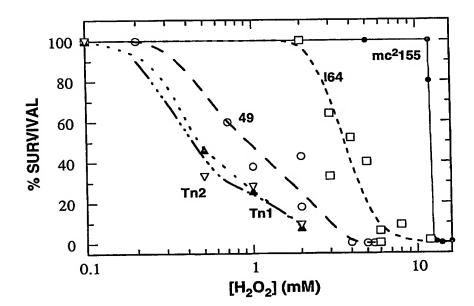


Figure 6

Figure 7

PCT/US03/11539

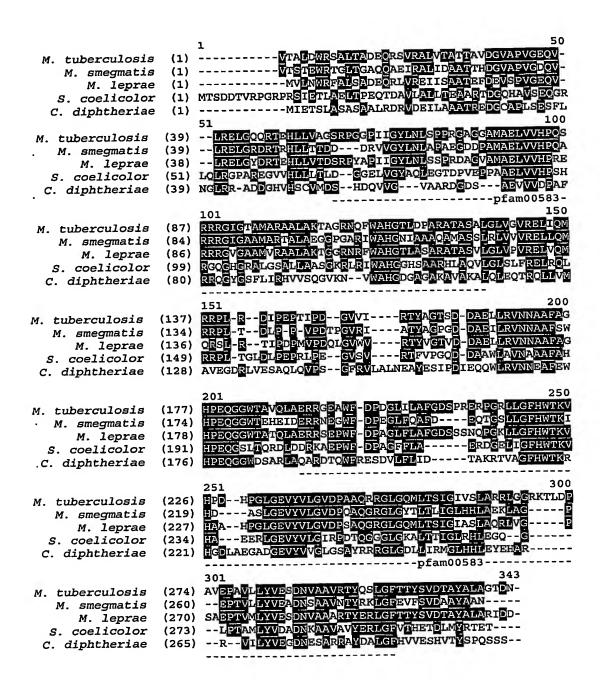
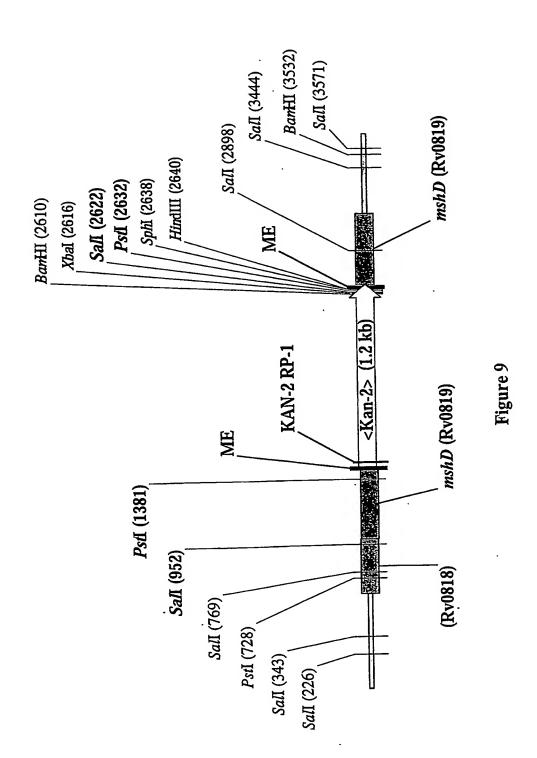


Figure 8



MshD amino acid sequence of M. tuberculosis (CAA17625.1) (Rv0819)

MTALDWRSALTADEQRSVRALVTATTAVDGVAPVGEQVLRELGQQRT EHLLVAGSRPGGPIIGYLNLSPPRGAGGAMAELVVHPQSRRRGIGTAMA RAALAKTAGRNQFWAHGTLDPARATASALGLVGVRELIQMRRPLRDIP EPTIPDGVVIRTYAGTSDDAELLRVNNAAFAGHPEQGGWTAVQLAERR GEAWFDPDGLILAFGDSPRERPGRLLGFHWTKVHPDHPGLGEVYVLGV DPAAQRRGLGQMLTSIGIVSLARRLGGRKTLDPAVEPAVLLYVESDNVA AVRTYQSLGFTTYSVDTAYALAGTDN (SEQ ID NO: 14)

Figure 10A

MshD amino acid sequence of M. smegmatis (PMshDMs-Tr)

VTSTEWRTGL TGAQQAEIRA LIDAATTHDG VAPVGDQVLR
ELGRDRTRHL LTTDDDRVVG YLNLAPAEGD DPAMAELVVH
PQARRRGIGA AMARTALAEG GPGARIWAHG NIAAAQAMAS
SLRLVVVREL LQMRRPLTDL PPVPDTPGVR IATYAGPGDD
AEILRVNNAA FSWHPEQGGW TEHEIDERRN EGWFDPEGLF
QAFDEQTGSL LGFHWTKIHD ASLGEVYVVG VDPQAQGRGL
GYTLTLIGLH HLAEKLAGPE PTVLLYVEAD NSAAVNTYRK
LGFEVFSVDA AYAAN (SEQ ID NO: 15)

Figure 10B

PCT/US03/11539

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MshD amino acid sequence of M. leprae (ML2193)

MVLNWRFALSADEQRLVREIISAATEFDEVSPVGEQVLRELGYDRTEHL LVTDSRPYAPIIGYLNLSSPRDAGVAMAELVVHPRERRRGVGAAMVRA ALAKTGGRNRFWAHGTLASARATASVLGLVPVRELVQMQRSLRTIPDP MVPDQLGVWVRTYVGTVDDAELLRVNNAAFAGHPEQGGWTATQLAE RRSEPWFDPAGLFLAFGDSSSNQPGKLLGFHWTKVHAAHPGLGEVYVL GVDPSAQGRGLGQMLTSIGIASLAQRLVGPSAEPTVMLYVESDNVAAA RTYERLGFTTYSVDTAYALARIDD (SEQ ID NO: 16)

Figure 10C

MshD amino acid sequence of *Streptomyces coelicolor* (SCD84.18c, SCO4151) MTSDDTVRPGRPRSIETLAELTPEQTDAVLALLTEAARTDGQHAVSEQG RLQLRGPAREGVVHLLLTLDGGELVGYAQLEGTDPVEPPAAELVVHPS HRGQGHGRALGSALLAASGKRLRIWAHGGHSAARHLAQVLGLSLFREL RQLRRPLTGLDLPEPRLPEGVSVRTFVPGQDDAAWLAVNAAAFAHHPE QGSLTQRDLDDRKAEPWFDPAGFFLAERDGELIGFHWTKVHAEERLGE VYVLGIRPDTQGGGLGKALTTIGLRHLEGQGLPTAMLYVDADNKAAVA VYERLGFVTHETDLMYRTET (SEQ ID NO: 17)

Figure 10D

MshD amino acid sequence of Corynebacterium diphtheriae (PMshDCd-Tr)

MIETSLASAS AALRDRVDEI LAAATREDGC APLSESFLNG
LRRADDGHVH SCVMDSHDQV VGVAARDGDS AEVVVDPAFR
RQGYGSFLIR HVVSQGVKNV WAHGDGAGAK AVAKALQLEQ
TRQLLVMAVE GDRLVESAQL QVPSGFRVLA LNEAYESIPD
IEQQWLRVNN EAFEWHPEQG GWDSARLAQA RDTQWFRESD
VLFLIDTAKR TVAGFHWTKR HGDLAEGADG EVYVVGLGSA
YRRRGLGDLL IRMGLHHLEY EHARRVILYV EGDNESARRA
YDALGFHVVE SHVTYSPQSS S (SEQ ID NO: 18)

Figure 10E

PCT/US03/11539

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Nucleic acid sequence mshD M. smegmatis, including stop codon

Figure 10F

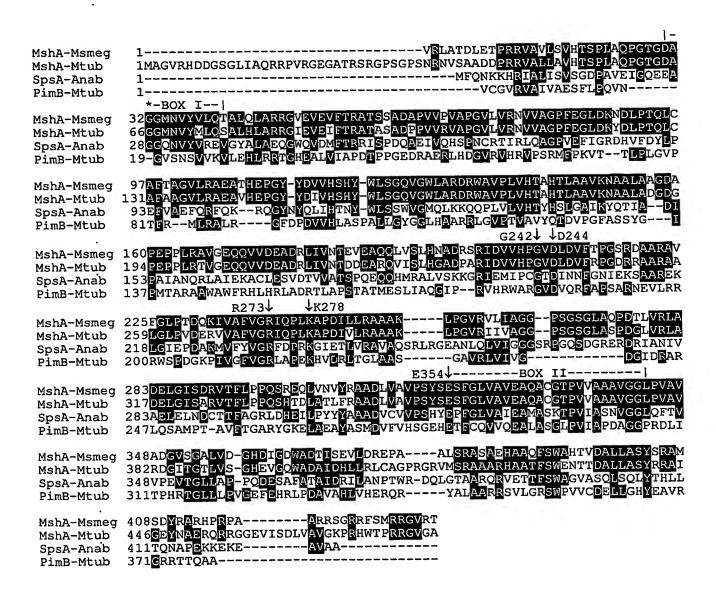


Figure 11

MshA amino acid sequence of M. smegmatis (PMshAMs-Tr)

VRLATDLETP RRVAVLSVHT SPLAQPGTGD AGGMNVYVLQ
TALQLARRGV EVEVFTRATS SADAPVVPVA PGVLVRNVVA
GPFEGLDKND LPTQLCAFTA GVLRAEATHE PGYYDVVHSH
YWLSGQVGWL ARDRWAVPLV HTAHTLAAVK NAALAAGDAP
EPPLRAVGEQ QVVDEADRLI VNTEVEAQQL VSLHNADRSR
IDVVHPGVDL DVFTPGSRDA ARAVFGLPTD QKIVAFVGRI
QPLKAPDILL RAAAKLPGVR VLIAGGPSGS GLAQPDTLVR
LADELGISDR VTFLPPQSRE QLVNVYRAAD LVAVPSYSES
FGLVAVEAQA CGTPVVAAAV GGLPVAVADG VSGALVDGHD
IGDWADTISE VLDREPAALS RASAEHAAQF SWAHTVDALL
ASYSRAMSDY RARHPRPAAR RSGRRFSMRR GVRT (SEQ ID NO: 19)

Figure 12A

NO: 20)

23/30

MshA amino acid sequence of M. tuberculosis (PMshAMtG1002)

MAGVRHDDGS GLIAQRRPVR GEGATRSRGP SGPSNRNVSA

ADDPRRVALL AVHTSPLAQP GTGDAGGMNV YMLQSALHLA

RRGIEVEIFT RATASADPPV VRVAPGVLVR NVVAGPFEGL

DKYDLPTQLC AFAAGVLRAE AVHEPGYYDI VHSHYWLSGQ

VGWLARDRWA VPLVHTAHTL AAVKNAALAD GDGPEPPLRT

VGEQQVVDEA DRLIVNTDDE ARQVISLHGA DPARIDVVHP

GVDLDVFRPG DRRAARAALG LPVDERVVAF VGRIQPLKAP

DIVLRAAAKL PGVRIIVAGG PSGSGLASPD GLVRLADELG

ISARVTFLPP QSHTDLATLF RAADLVAVPS YSESFGLVAV

EAQACGTPVV AAAVGGLPVA VRDGITGTLV SGHEVGQWAD

AIDHLLRLCA GPRGRVMSRA AARHAATFSW ENTTDALLAS

YRRAIGEYNA ERQRRGGEVI SDLVAVGKPR HWTPRRGVGA (SEQ ID

Figure 12B

Nucleic acid sequence mshA M. smegmatis, including stop codon

## **GTGCGTCTAGCGACAGACCT**

CGAGACCCCCGCGCGTGGCGTGTTGTCGGTACACACCTCTCCGC TGGCGCAGCCGGCACCGGCGACGCGGCATGAACGTCTACGT GTTGCAGACCGCGCTGCAACTGGCCCGGCGTGGCGTCGAGGTCGAG GTCTTCACCAGGGCCACGTCGTCGGCCGATGCGCCGGTCGTGCCTGT GGCGCCCGGTGTGCTGCGCAACGTCGTGGCCGGCCCGTTCGAAG GCCTCGACAAGAACGATCTGCCCACGCAGCTGTGCGCGTTCACCGCG GGTGTGCTGCGCCGAGGCGACCCACGAGCCCGGCTACTACGACG CGCGACCGCTGGCCGTGCCGCTGGTGCACACCGCGCACACGCTGG CCGCGGTCAAGAACGCCGCACTCGCCGCGGGCGACGCACCCGAGCC GCCGCTGCGCGCGTGGGCGAACAACAGGTGGTCGACGAGGCCGAC CGCCTCATCGTGAACACCGAAGTCGAAGCGCAGCAACTGGTCTCGTT GCACAATGCCGACCGCTCACGCATCGACGTCGTGCACCCCGGCGTCG TTCGGGCTTCCCACCGACCAGAAGATCGTGGCGTTCGTGGGCCGCAT CCAGCCGCTCAAGGCCCCCGACATCCTGCTGCGTGCCGCGGCGAAAC TGCCCGGCGTGCGGTGCTGATCGCCGGTGGACCCTCCGGATCGGGA CTTGCCCAACCGGACACGCTGGTTCGGCTCGCCGACGAACTGGGTAT CAGTGACCGGGTGACGTTCCTCCCGCCGCAGAGCCGCGAACAACTG GTCAACGTGTACCGGGCGGCCGATCTGGTCGCGGTGCCGAGCTACTC CGAGTCGTTCGGCCTGGTCGCCGTCGAGGCGCAGGCGTGCGGCACGC CCGTCGTCGCCGCCGTCGCCGACTCCCGGTCGCCGAC GGCGTCAGCGGGCACTCGTCGACGGCCACGACATCGGCGACTGGG CCGACACCATCAGCGAGGTGCTCGACCGCGAGCCCGCCGCGCTGAG CCGCGCCTCCGCCGAACACGCCGCTCAGTTCTCGTGGGCGCACACCG TCGACGCGCTGCTCGCCAGCTACAGCCGGGCCAT GACGCCGGTTCTCGATGCGCAGGGGAGTACGCACGTGA (SEQ ID NO: 49)

Figure 12C

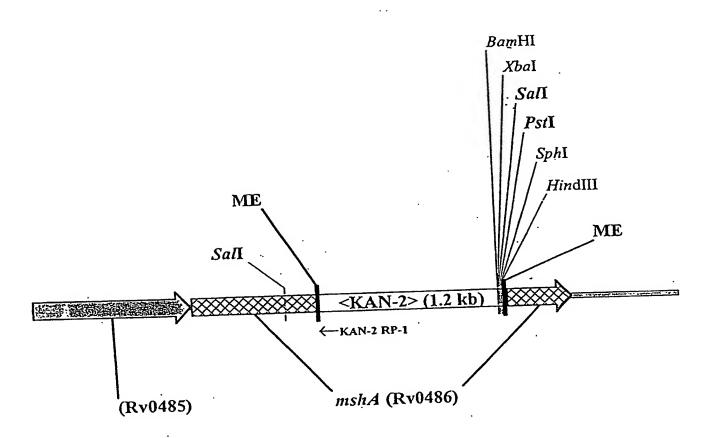


Figure 13

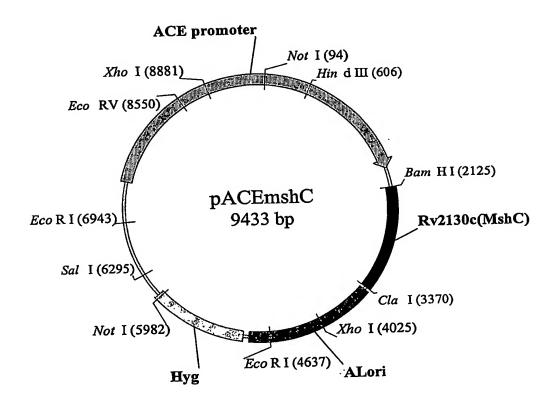


Figure 14

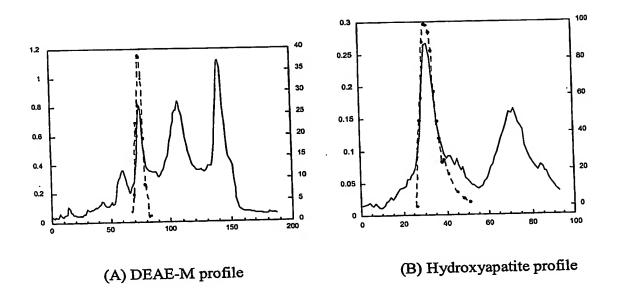


Figure 15

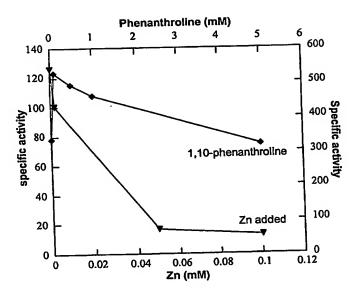


Figure 16

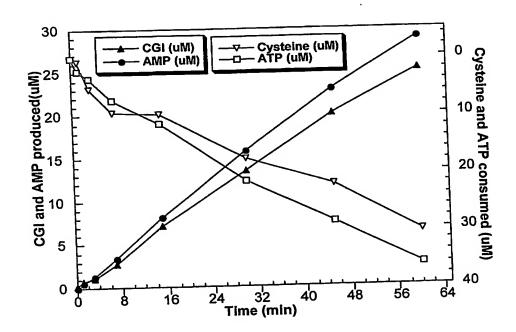


Figure 17

## (a) First Half of Rossman fold:

M. smeg MshC		C.strt.MshC	T. bifd. MshC	M. tubr CvsS	E. coli CysS

# (b) Second half of Rossman Fold:

(215) GTLGRGRPGWHIECVAIALDHLGMGFDVQGGGSDLAFPHHEMGASHAQALT (219) SPFGPGRPGWHVECSAIATNRLGSHFAIQGGGSDLAFPHHEFSAAHAEAAL (198) TPLGRGRPGWHVECSAISVHELGMGFDLNGGGDDLIFPHHEMGAAEACCAT (214) TPWGRGRPGWHLECSAMARSYLGPEFDIHCGGMDLVFPHHENEIAQSRAAG (190) SPFGPGRPGWHVECAAIALSRIGIGLDIQGGGSDLIFPHEFTAAHAECVR (196) SPWGAGRPGWHIECSAMNCKQLGNHFDIHGGGSDLMFPHHENETAQSTCAH (218) SPFGRGRPGWHVECSAIALTRIGTGLDIQGGGSDLIFPHHEYSAAHAESVT CysS M. smeg MshC C.strt.MshC T.bifd.MshC M. tubr CysS M. lepr MshC S.coel.MshC E. coli

GERRFARHYV <b>H</b> TGMIGWDGH <b>KMSKS</b> (293)	GERRFARHYVHAGMIGWDEHKMSKS (265)	GEFPMAKAYVHAGMVGLDGEKMSKS (290)	KVERMAGHYVHAGMIALDGVKMSKS (294)	GSRPQARHYLHVAMVGLDGEKMSKS (289)	DGFARYWLHNGWVTMGGEKMSKS (271)	DGQ-YVNYWMHSGMVMVDREKMSKS (270)
M. smed MshC	M. lepr Mshc	S. coel. MshC	C. strt. MshC	T.bifd.MshC	M. tubr CysS	E.coli CysS

Figure 18

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